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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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06/325, 070 10/20/96 CROUCH

1805 17

1805/0700

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EXAMINER

GUZO, D

ART UNIT

PAPER NUMBER

1805

17

DATE MAILED:

02/03/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 10/15/96 and 9/19/96

☐ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three (3) month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1, 3, 6-15 and 32-37 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1, 3, 6-15 and 32-37 is/are rejected.

☒ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

- SEE OFFICE ACTION ON THE FOLLOWING PAGES -

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1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 32-33 and 35-37 are rejected under 35 U.S.C. § 102(a) as being anticipated by Bacchetti et al.

Applicants claim a replication defective, recombinant adenoviral vector comprising a tumor suppressor gene (p53) and lacking an essential gene such as E1A, E1B, etc.

Bacchetti et al. (Inter. J. Oncol., Vol 3, pp. 781-788, 1993, see whole article, particularly Fig. 1; cited by applicants) recites the generation of a replication defective, recombinant adenoviral vector comprising a p53 gene and lacking the E1 region. Therefore, Bacchetti et al. teaches the claimed invention. It is noted that, according to the Inter. J. of Oncology, the issue containing the Bacchetti et al. article was publicly available as of 10/22/93.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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4. Claims 1, 3, 7, 8, 10 and 12-14 are rejected under 35 U.S.C. § 102(b) as being anticipated by Haj-Ahmad et al.

This rejection is maintained for reasons of record in the previous Office Action (Paper #8) and for reasons outlined below.

Applicants traverse this rejection by asserting that a deletion up to 3827 nucleotides is not "about 4000" because there is a functional difference between deletions of 3827 and "about 4000" nucleotides with regard to recombination in 293 cells. Applicants also have amended Claim 1 to indicate that the total length of the vector DNA is less than about 35 KB and indicate that the claims as amended are not anticipated by Haj-Ahmad et al.

5. Applicant's arguments filed 9/19/96 have been fully considered but they are not deemed to be persuasive.

Applicants, in the instant specification, do not define the term "about 4000" nucleotides. The only definitions of what "about 4000" nucleotides means with regard to the deletion size in the instant specification are present on page 16: "Also provided by this invention is a recombinant adenovirus expression vector, as described above, having less extensive deletions of the protein IX gene sequence extending from 3500 bp from the 5' viral termini to approximately 4000 bp, in one embodiment." From this language, the ordinary skilled artisan, reading the specification and without any further guidance, would interpret

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the "about 4000" bp recited in the claims to mean deletions from 3500 to "approximately" 4000 bp (See also MPEP 2173.05(b)).

With regard to the size of the adenoviral vector being smaller than the vector recited by Haj-Ahmad et al., it is unclear if applicants are reciting the size of the vector DNA without a foreign gene inserted into it or whether applicants are reciting the size of the vector DNA plus the DNA of the inserted foreign gene. If applicants are claiming the size of the vector DNA without an inserted foreign DNA sequence, then it is noted that Haj-Ahmad et al. teach a vector with 5.5 kb of DNA deleted compared to the wild type virus, therefore their vector is approximately 30.5 KB (See Haj-Ahmad et al., page 272, 2nd paragraph of the Discussion). If applicants, on the other hand, are claiming the vector plus a foreign gene being about 35 KB in size, then it is noted that the vector recited by Haj-Ahmad et al. could accommodate up to potentially 7.5 KB of foreign DNA and DNAs of any size smaller than 7.5 KB, indeed, Haj-Ahmad et al. recites insertion of a 4 KB insert into the d1E1,3 vector, producing a vector of approximately 34.5 KB (See page 272, 2nd paragraph of the Discussion section).

6. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section

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102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

7. Claims 6 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Haj-Ahmad et al. in view of Winnacker.

8. Claims 11 and 15 are rejected under 35 U.S.C. § 103 as being unpatentable over Haj-Ahmad et al. in view of Bacchetti et al.

These rejections are maintained for reasons of record in the previous Office Action and for reasons outlined below.

Applicants traverse these rejections by essentially reiterating the arguments made against the Haj-Ahmad et al. reference (in the traverse of the 35 USC 102(b) rejection) and further indicating that the Winnacker and Bacchetti et al. references do not cure the defects of the Haj-Ahmad et al. reference. Applicants also indicate that the deletion of the protein IX polyA signal is not taught or suggested by the prior art.

Applicants arguments have been carefully considered but are not deemed to be persuasive. Since applicants' traverse of the

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instant 35 USC 103 rejection is predicated upon arguments made against the Haj-Ahmad et al. reference and since said arguments have been fully addressed in the instant Office Action (See the above 35 USC 102(b) rejection), the instant rejections under 35 USC 103(a) stand for reasons of record. With regard to the substitution of a heterologous polyA signal for the deleted protein IX polyA signal, it appears that the substitution of one polyA signal for another in the context of the claimed vectors does not affect in any discernable fashion the activity of the vector (applicants provide no evidence in the instant specification that this substitution of one polyA signal for another functionally equivalent polyA signal affects the activity of the vector in any fashion) or differentiate it from the prior art vectors in any significant, non-obvious, fashion.

9. Claims 32-37 are rejected under 35 U.S.C. § 103 as being unpatentable over Haj-Ahmad et al. as applied in the above rejections of Claims 6 and 9 and 11 and 15 and further in view of Casey et al.

Applicants recite replication defective adenovirus vectors containing a tumor suppressor gene (i.e. p53) and containing deletions in one or more essential genes.

Haj-Ahmad et al. is applied as above.

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Casey et al. (See whole document, particularly the Abstract and page 1791, 1st three paragraphs) recites the tumor suppressor activity of the p53 gene product and the possibility that delivery of the p53 gene to cells may suppress the growth of some tumors.

It would have been obvious for the ordinary skilled artisan, seeking to develop a composition for delivery of genes of interest to target cells to use the adenoviral vectors of Haj-Ahmad et al. to deliver a tumor suppressor gene such as p53 to target cells because Casey et al. indicates that the p53 gene has been delivered to tumor cells using retroviral vectors and has resulted in some suppression of cancer cell growth. The ordinary skilled artisan would have been motivated to substitute the adenoviral vectors (instead of retroviral vectors) recited by Haj-Ahmad et al. for the known and expected properties of said vectors (i.e. they can accommodate a large insert, they are easy to grow, they infect a wide range of tissues, etc.). Given the well known teachings of the prior art on adenoviral vectors and tumor suppressor genes such as p53, it must be assumed that the ordinary skilled artisan would have had a reasonable expectation of success in generating the claimed vectors. Absent unexpected results it must be assumed that the instant invention is *prima facie* obvious.

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10. Claims 1, 3, 6-15 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants recite in Claim 1 adenoviral vectors having deletions of from "about 360" nucleotide to "about 4000" nucleotides. The metes and bounds of the claimed subject matter is unclear because there is no indication in the specification as to what size deletions are covered by the term "about". As noted in MPEP 2173.05(b), claims reciting relative terms such as "about" are indefinite if there is close prior art and there is nothing in the specification or prosecution history to provide an indication as to what range is covered by a relative term such as "about".

Claim 7 is objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim must refer to other claims in the alternate only. See M.P.E.P. § 608.01(n).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mindy Fleisher, can be reached on (703) 308-0407. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

David Guzo
January 31, 1997


DAVID GUZO
PRIMARY EXAMINER
GROUP 1800